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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,550	02/09/2001	Akihiro Funakoshi	053466/0299	5276

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/762,550	FUNAKOSHI ET AL.	
	Examiner	Art Unit	
	Lorraine Spector	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16-23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 16-23, 25, 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 14, 16-23, 25 and 26 are pending and under consideration. There have been no amendments to the claims since the response of 8/15/07.

With regard to the Examiner's statement in the previous Office Action that applicants have not made *any* of the exhibits of record in an IDS such is not a requirement to file an IDS, it is noted that applicants are required to make known to the examiner any art of which they are aware that would have a bearing on patentability. The references in question were *not* cited to establish the "level of skill in the prior art", but rather were submitted to establish (although non-persuasively) what the *preponderance of evidence in the art pertaining to the claimed invention is.* Accordingly, applicants *should* have cited at least the Norman reference on an IDS, just as the Examiner cited references on a form PTO-892.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 16-23, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of

direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is the use of IL-6 inhibitors to treat acute pancreatitis. The exhaustive prosecution has established that both IL-6 and TNF are associated with acute pancreatitis, that IL-6 inhibits TNF-alpha, and TNF-alpha induces IL-6.

The prior art does not recognize IL-6 inhibitors as a treatment for acute pancreatitis, and presents information that does not give a clear picture of whether such treatment would be successful. As stated in the previous rejection under §103, Gross et al. teach that IL-6 concentrations are associated with acute pancreatitis; see page 525. Farkas et al. teach that experimental acute pancreatitis results in increased blood-brain barrier permeability (title), and that such is associated with increased IL-6 levels (page 149, paragraph bridging columns). Accordingly, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the compositions taught by Sato et al. or Kishimoto et al. to treat acute pancreatitis, in view of the teachings of Gross et al. and Farkas et al. The person of ordinary skill in the art would have expected success at doing so because the primary references teach the antibodies for the express purpose of inhibiting IL-6 associated responses.

At page 2 of the response filed 7/6/09, applicants argue that a Wikipedia entry on IL-6 shows that IL-6 is both a pro-inflammatory and an anti-inflammatory cytokine. The Examiner notes that applicants have not made *any* of the exhibits of record in an IDS. The first page of the Wikipedia entry is illegible. The paragraph bridging pages 1-2, of which the Examiner can only read the portion on page 2 clearly indicates that IL-6 is a pleiotropic cytokine, having different actions in different situations. Therefore, the argument that it can be either pro-inflammatory or anti-inflammatory, without a more careful examination of *when* it has which activity, is not probative. On the second page, the entry states, under "Functions of IL-6", that "IL-6 is one of the most important mediators of fever and of the acute phase response." This would directly suggest administration of IL-6 inhibitors for acute phase responses, such as acute pancreatitis.

Exhibit B, a discussion of positive and negative feedback is not directly applicable to the arguments at hand, and merely provides basic definitions of basic terms.

Aderka et al. teaches that IL-6 inhibits TNF-alpha, and, as characterized by applicants, would suggest the administration of IL-6, and not inhibitors of such. Aderka was using an LPS-induced sepsis model, and not a model of acute pancreatitis.

Ulich, as characterized by applicants, teaches that If IL-6 is acting as an anti-inflammatory cytokine as part of an endogenous negative feedback loop, the person of ordinary skill in the art would expect that IL-6 would occur later in inflammation, rather than earlier. Ulich was using a model of intratracheal injection of endotoxin, and not a model of acute pancreatitis.

The Examiner takes no issue with applicants characterization of Norman et al.

Thus, while the Examiner has made a case *for* inhibition of IL-6 in acute pancreatitis (see 103 rejection in previous Office Actions), applicants have made a case *against* such.

Accordingly, there is no consensus in the art.

In this particular case, given the teachings in the art, there is no predictability about *whether* administration of IL-6 would be beneficial to patients having acute pancreatitis, nor *how and when* such should be administered; clearly, looking at the most recent reference cited by applicants in their most recent submission, timing would be critical.

There are *no* working examples in which *any* anti-IL-6 molecule was administered to *any* animal or human either having acute pancreatitis, or an accepted model of such.

The claims do not specify how or when the active agent is to be administered.

Accordingly, the Examiner concludes that it is not predictable that the claimed invention would work *at all*. Nor is there sufficient disclosure to allow the skilled artisan to practice the claimed invention without substantial experimentation. All applicants have presented is the germ of an invention, and an invitation to determine how to practice that invention.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentec, Inc, v. Novo Nordisk, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot, following the guidance presented therein, practice the suggested method without first making a substantial inventive contribution.

At page 3 of the response filed 2/23/10, applicants argue that the Examiner is using *prior* art to establish unpredictability, and is ignoring the evidence in the specification. This argument has been fully considered but is not deemed persuasive because as stated in MPEP 2164.03, "What is known in the art provides evidence as to the question of predictability", citing *In re Marzocchi,* 439 F.2d 223-224, 169 USPQ 367, 369-70 (CCPA 1971).

With respect to Example 1, page 29 of the specification, the first paragraph clearly states: "An anti-mouse IL-6 receptor monoclonal antibody MI6-1 was administered to the mice at 1 mg/mouse via the tail vein immediately before caerulein administration." Thus, the example relates to *prevention*, not *treatment* of acute pancreatitis. Inhibiting IL-6 *prior to the development of acute pancreatitis* is in no way predictive of what will happen if the same is done to a patient who already *has* the condition; once the disease process initiates, as evidenced by the references, numerous cytokines are released, some as part of cascade reactions. While Example 1 may show that IL-6 is essential to the *development* of acute pancreatitis, it has no bearing on the treatment of such. According to MPEP 2164.04, the standard for enablement "is for the examiner to give reasons for the uncertainty of the enablement". It is noted that although applicants have dismissed the teachings of the prior art as used by the examiner, they have used the prior art in rebutting the Examiner's findings. Further, although applicants dismiss the teachings of the prior art, they cannot produce "non"-prior art to substantiate their assertions,

either. Also in MPEP2164.04, it is stated that "References should be supplied if possib le to support a *prima facie* case of lack of enablement…", once again citing the *Marzocchi* case. This is exactly what the Examiner (and applicants) have done.

At page 4 of the response, applicants argue that cerulean-induced acute pancreatitis is an accepted model system. This argument has been fully considered but is not deemed persuasive because in Example 1, the treatment was given *before* the cerulean was administered, and hence *before* the acute pancreatitis developed The same is the case in Example 2. Thus the examples are not considered by the Examiner to be "working" examples, as they do not relate to the claimed invention. Such is not the case in the references cited by applicants at page 4 of the response, as characterized by applicants.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday from 8:00 A.M. to 4:30 P.M., and Tuesday, Thursday and Friday, 8:00 A.M. to 2:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Gary Nickol, at telephone number 571-272-0835.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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